Abstracts of Original Contributions: 46th Annual Scientific Session

The American College of Cardiology is pleased to announce that nearly 6,800 abstracts of original contributions were submitted to the Program Committee of the 46th Annual Scientific Session. Space and time considerations this year allowed the selection of 2,260.

Each abstract was peer reviewed by a panel of graders; chosen abstracts are presented in either oral or poster format.

The American College of Cardiology thanks the thousands of abstract participants and the hundreds of category graders and chairs for their efforts.

Carl V. Leier, MD, FACC
Chair
1997 Annual Scientific Session Program Committee

Robert J. Cody, MD, FACC
Co-Chair
1997 Annual Scientific Session Program Committee

901 Myocardial Ischemia and Vascular Interactions

Sunday, March 16, 1997, 5:00 p.m.–7:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 5:00 p.m.–7:00 p.m.

901-31 Does Ischemic Preconditioning (IP) Require Reperfusion Before the Sustained Ischemia?

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IP is generally thought to be initiated through several bouts of ischemia and reperfusion that precede a prolonged ischemic event. To test whether a reperfusion period must precede this final ischemic event, one series without reperfusion (intraischemic preconditioning: IIP) was compared to conventional IP (CIP). *Methods:* Experiments were performed on 19 isolated rabbit hearts that were connected to a modified Langendorff apparatus. The hearts were perfused with an erythrocyte suspension (Hct = 30%; Ca^{2+} = 1.8 mM). Protocol: (1) control series (n = 5): 60 min normal flow → 60 min low flow (10%) ischemia → 60 min reperfusion. (2) CIP series (n = 7): control → 4 times 5 min of zero flow with 10 min reperfusion → 60 min low flow (10%) ischemia → 60 min reperfusion. (3) IIP series (n = 7): control → 50 min normal flow → 10 min no flow → 60 min low flow (10%) ischemia → 60 min reperfusion. At the end of each protocol, the hearts were cut into 6 to 9 slices and stained with TTC. The infarcted area was assessed by computer-aided planimetry. *Results:* (means ± SD): The infarct size in control hearts was 6.3 ± 3.7% from LV total cardiac mass, in CIP hearts 2.6 ± 1.8% and in the IIP hearts 3.1 ± 1.3%. In the model used, CIP exerted a statistically significant ($p < 0.05$) protective effect. IIP exerted a similar effect that was, however, less pronounced. In the model used, the preconditioning effect appears to not depend on reperfusion and thus, the protective mechanism of preconditioning to develop during the initial ischemia that precedes the sustained ischemia. Alternatively, low flow ischemia always encompasses some reperfusion.

901-32 Identification of 5 Hypoxia-Inducible RNA-Protein Binding Sites Conserved in Rat and Human Vascular Endothelial Growth Factor mRNA

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The hypoxic induction of vascular endothelial growth factor (VEGF), a potent angiogenic factor, is due in large part to an increase in the stability of its mRNA. We have previously demonstrated the presence of a hypoxia-inducible protein complex (HIPC) which binds to a region of the 3′ untranslated region (UTR) of the rat gene for VEGF that is critical for the stabilization of VEGF mRNA in an *in vitro* RNA degradation assay. In order to identify other regions of functional importance in the 3′ UTR of VEGF mRNA we sequenced the corresponding region for the human VEGF gene and compared it with the rat sequence. We found that all four potential polyadenylation sites are conserved as are the two consensus nonameric (UUAUUUAUU) instability elements that we have previously shown to mediate the rapid turnover of VEGF mRNA under normoxic conditions. Alignment of the region previously shown for rat VEGF mRNA to be critical for its stabilization by hypoxia with the corresponding human VEGF mRNA sequence demonstrated a greater than 90% sequence homology. Furthermore, RNA electromobility shift assay (EMSA) identified five HIPC binding sites in the human and rat VEGF 3′ UTR that are conserved. RNA EMSA cross-competition studies between each of the HIPC binding sites demonstrated that they are each capable of independently binding a similar if not identical HIPC. These data further support the role of this HIPC in mediating the stabilization of VEGF mRNA by hypoxia and represent a critical step in developing novel new strategies to treat human conditions resulting from vascular insufficiency.

901-33 Regular Ethanol Consumption Protects Against Myocardial Ischemia-Reperfusion Injury by Activation of Protein Kinase C

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Recent studies suggest that regular ethanol intake (EtOH) improves outcomes after coronary events. Attenuation of ischemia-reperfusion (IR) injury, as seen with ischemic preconditioning, is a mechanism which could account for these improved outcomes. Therefore we tested the hypotheses that 1) EtOH attenuates IR injury, and 2) this protective effect is mediated by activation of protein kinase C (PKC). Guinea pigs were pair-fed nutritionally supplemented liquid diets (calorically matched) with 15 or 0% ethanol-derived calories for 10 weeks. Perfused hearts were subjected to 45 min global ischemia and 48 min reperfusion in the presence or absence of the PKC inhibitor, chelerythrine (CHE, 10 μM). LV function was monitored by LV developed (LVP) and diastolic (LVEDP) pressures. Release of creatine kinase (CK) was used as an index of myocyte injury. *Results:* Body weights of EtOH and controls (CTL) were not different. After IR, EtOH had a greater recovery of LVP, less rise of LVEDP and less CK release, compared to CTL. CHE abolished the cardioprotective effect of EtOH. *Conclusion:* EtOH attenuates myocardial IR injury through PKC activation, in a manner analogous to ischemic preconditioning.

	Pre-ischemia		48 min Reperfusion		
	LVP (mmHg)	LVEDP (mmHg)	LVP	LVEDP	CK (U/g.ml)
CTL	117 ± 4	10 ± 0	25 ± 4	58 ± 5	469 ± 74
EtOH	117 ± 2	10 ± 0	49 ± 4*	35 ± 6*	260 ± 40*
CTL + CHE	121 ± 3	10 ± 0	24 ± 3	53 ± 4	484 ± 44
EtOH + CHE	118 ± 3	10 ± 0	30 ± 3	49 ± 4	415 ± 42

(mean ± SEM, *$p < 0.05$ vs. CTL, n = 9 for each group)